Mechanisms of concanavalin A-induced inflammation in the rat

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Concanavalin A (Con A), a mitogenic lectin derived from the jack bean, has been shown to stimulate lymphocytes to produce soluble mediators known as lymphokines (Pick, Brostoff, Krejci & Turk, 1970). Lymphokines have been implicated in the mediation of chronic inflammatory processes (e.g. Pick & Turk, 1972) and consequently it was of interest to establish (a) whether Con A induced an inflammatory response after administration to the rat hind paw and (b) whether the substances mediating the response resembled those produced by more widely used phlogogenic agents.

Male Wistar rats (CE/CFHB strain, 80-100 g) were used in these experiments. Con A was dissolved in 0.9% saline (w/v) and injected in 0.1 ml volumes via the subplantar route into the right hind paw. The contralateral paw received an equal volume of saline. The mean difference between both paws, as measured by mercury displacement plethysomography, was determined at various time intervals.

Con A produced a dose related (0.01-1.0 mg/paw) paw oedema that was slow in onset reaching a maximum by 24 h and still present at 72 hours. Both cyproheptadine (10 mg/kg, s.c.), a histamine and 5-hydroxytryptamine (5-HT) antagonist, and methysergide bimaleate (2.5 mg/kg, s.c.), a 5-HT antagonist, administered separately 30 min before Con A significantly suppressed Con A–induced oedema up until 3 hours. However, the antihistamine, mepyramine maleate (2.5 mg/kg, s.c.) administered 30 min before Con A, was without effect. Soyabean trypsin inhibitor (SBTI; 80 mg/kg, s.c.) which depresses kinin levels (Webster, Maling, Zweig, Williams & Anderson, 1972), administered 30 min prior to Con A inhibited the oedema almost completely up to 6 hours. Moreover, in separate experiments, kinin-like activity was measurable from air-blebs produced by the injection of air (after Willis, 1969) followed by 7.5 mg Con A in 5 ml saline. This was maximal at 16 hours.

Indomethacin (5 mg/kg) and aspirin (200 mg/kg), anti-inflammatory drugs capable of inhibiting prostaglandin production, administered subcutaneously 60 min before Con A both inhibited the oedema. This inhibition was approximately 30% for both drugs at 4 hours. Prostaglandin-like activity is also measurable by bioassay on the rat fundic strip (Piper & Vane, 1969) in extracts from Con A-air blebs (7.5 mg per rat) taken at intervals over a 24 h period and was maximal at 16 hours.

Thus 5-HT, kinins and prostaglandins appear to act as mediators of Con A-induced oedema although histamine does not appear to play a role in this response. Since a combination of cyproheptadine, SBTI and indomethacin does not completely abolish the Con A oedema this residual response is likely to be mediated by other factors such as complement and constituents of cellular infiltrates that are not affected by such drug treatment.

References

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